istence of these particular hydrophobic bonds is manifested in deoxygenated, concentrated hemolysates by reversible sol-gel transformations at 0° and 37°C. Deoxygenated hemolysates of S hemoglobin gel at 37°C and liquefy at 0°C. In such systems, demonstration of reversible, temperature-dependent sol-gel transformations (a negative temperature coefficient of gelation is specific for S hemoglobin or the S structural variant, hemoglobin C (Harlem). The test is simple, has clear end-points, will detect both homozygous and heterozygous S hemoglobin, and is specific.

The molecular mechanism for sickling of hemoglobin S has been so precisely defined by the Murayama hypothesis that by extension we have selected on theoretical grounds urea as a chemical desickling agent. Urea attacks intertetrameric hydrophobic bonds implicated by Murayama to break those specific pathogenetic bonds formed in part by the substituted valine residues. Urea forms new hydrophobic bonds of its own with the improperly structured hemoglobin S tetramer, altering the steric structure of the hemoglobin S molecule WITHOUT adversely affecting the vital function of oxygen transport. Thus, by chemical manipulation, a lethal molecular property is inhibited by steric hindrance with the formation of urea-hemoglobin complex, since tetrameric polymerization or "stacking," that is, sickling, is impossible.

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Value of Histochemistry in the Investigation of Human Muscle Diseases

Awareness of the value of histochemical techniques in the investigation of human neuromuscular disorders has increased in the last few years. Such studies have allowed the definition of two or more fiber types, recognition of abnormalities in the reactivity and localization of biochemically defined organelles, determination of the magnitude of collateral reinnervation from type-specific fiber grouping and precise identification of regenerative activity and inflammation.

With such procedures, significant advances have been made in our understanding of the identification and pathogenesis of unusual muscle disorders including nemaline, central core, myotubular and vacuolar myopathy. Increased use of morphometric analysis of fiber types has proved of prognostic and therapeutic value. Newer approaches have placed emphasis on the recognition of the differential susceptibility of fiber types to degeneration or atrophy in a variety of neurogenic and myopathic disorders. Further advances in the recognition and investigation of myopathies will require the continued association of clinician and pathologist.

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Prenatal Diagnosis of Inherited Diseases

A specimen of amniotic fluid (about 10 ml) taken between the 14th and 16th week of pregnancy contains viable cells of fetal origin. The sex of the fetus, chromosomal abnormalities and certain enzyme defects can be diagnosed from these cells after two to four weeks in cell culture. The combined maternal and fetal risk of amniocentesis (probably less than 1 percent) is substantially less than the risk of giving birth to an affected child in families at risk for a detectable genetic disorder (25 percent) or in pregnancies occurring in women over 40 years of age (3 percent). The procedure is not universally applicable, however; not all genetic diseases, and none of the dominant or polygenically inherited disorders, can be detected. The

overall success rate is about 75 percent even under optimal conditions of cell culture and analysis. Physicians must bear in mind that diagnostic amniocentesis should be undertaken with the understanding that abortion is the only available therapy.

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Status of C Type Virus in Cat Tumors

C type RNA tumor viruses are proved to be the causative agents of malignant lymphoma and sarcoma in domestic cats. The incidence of feline lymphoma is four to five times greater in cats than in humans. There is no convincing evidence for infectious spread of these agents under natural conditions between cats or from cats to other animals or to man. Evidence suggests but does not prove that the C type virus genome is inheritable, presumably in the form of DNA.

House cats differ from other randomly bred vertebrate species in showing a marked degree of spontaneous expression of their latent C type virus genome in the form of group-specific antigen and replicating C type particles.

A human sarcoma cell line, previously free of C type virus particles, started to produce large numbers of such virus particles after transplantation into a fetal kitten. This virus (RD-114) proved to be no known cat or other mammalian C type virus and may thus be wholly or partially of human origin.

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McAllister R, Nicholson M, Gardner M, et al: C-type virus released from cultured human rhabdomyosarcoma cells. Nature (in press)

Evaluation of Hepatotoxicity by Electron Microscopy

Examination of liver biopsy material with the electron microscope can be a useful aid in studying the potential hepatotoxicity of drugs and environmental toxins. Light microscopy frequently reveals only minimal fatty changes, not necessarily indicative of liver abnormality. Ultrastructural studies, however, often disclose proliferation of the smooth endoplasmic reticulum as well as mitochondrial enlargement; also, crystalline inclusions may be found within the mitochondrial matrix. Other alterations include the development of autophagosomes, pigment inclusions, and, with some compounds, increased numbers of microbodies. Proliferation of the smooth endoplasmic reticulum is associated with increased activity of some of the enzymes located in the microsomal fraction.

Although all of these changes have been found in apparently healthy persons, their presence should alert the physician to the possibility of hepatic injury.

Recent studies on the hepatoxicity of methotrexate indicate that abnormalities may persist for months or even years after the hepatotoxin is withdrawn.

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Lymphomatoid Granulomatosis

Lymphomatoid granulomatosis is a lymphoproliferative disorder associated with angiitis and granulomatosis of the lung, resembling and possibly related to Wegener's granulomatosis. The pulmonary lesions are usually multiple, bilateral